

FACTOR XIa INHIBITION WITH ASUNDEXIAN IN ACUTE NON-CARDIOEMBOLIC STROKE OR HIGH-RISK TRANSIENT ISCHEMIC ATTACK: PRIMARY RESULTS OF THE OCEANIC-STROKE TRIAL

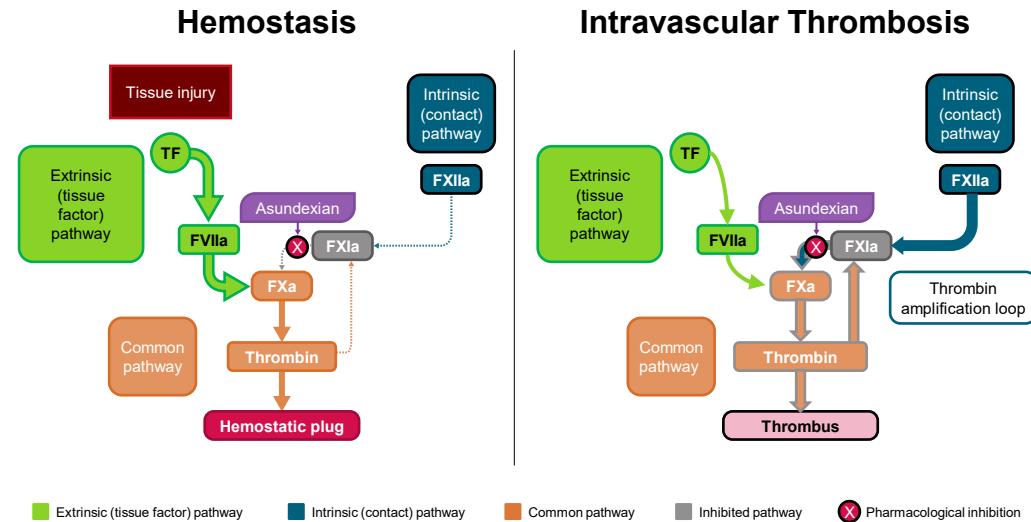
M. Sharma, Q. Dong, T. Hirano, S. Kasner, J. Saver, J. Masjuan, A. Demchuk, C. Cordonnier, D. Bereczki, G. Tsivgoulis, R. Veltkamp, I. Staikov, H-J. Bae, B. Campbell, A. Zini, I-H. Lee, S. Ameriso, M. Kovar, R. Mikulik, R. Lemmens, J. Ferro, T. Robinson, H. Christensen, S. Ozturk, R. Leker, P. Turcani, A. Slowik, P. Amaya, F.K. Hoo, G.M. De Marchis, M. Knoflach, P.N. Sylaja, J. Putaala, J.M. Coutinho, H.B. van der Worp, E. Miglane, V. Matijosaitis, A.G. Lindgren, G. Sampaio Silva, E. Sandset, S. Turuspekov, P. Amarenco, K. Sheth, E.E. Smith, J. Eikelboom, R. Joudi, K. Schulze, L. Xu, L. Heenan, C. Neumann, J. Gilbride, E. Muehlhofer, P. Colorado, L. Keller, H. Mundl, A. Shoamanesh for the OCEANIC-STROKE Steering Committee and Investigators

DISCLOSURES

M.S. declares consulting for Bayer, Regeneron and Anthos; research funding for the current study from Bayer paid to his institution; research funding from BMS and Janssen.

BACKGROUND

- Genetic FXI deficiency associated with:
 - reduced risk of ischemic stroke
 - without increased risk of ICH¹⁻³
- FXI has a minor role in hemostasis but may increase pathologic thrombosis
- Potential to uncouple hemostasis from thrombosis makes FXIa an attractive therapeutic target



Dashed arrows indicate minimal involvement of FXIa in hemostasis.
Figure adapted from Sharma M, et al. *European Stroke Journal*. 2026;11(1):aakaf017.

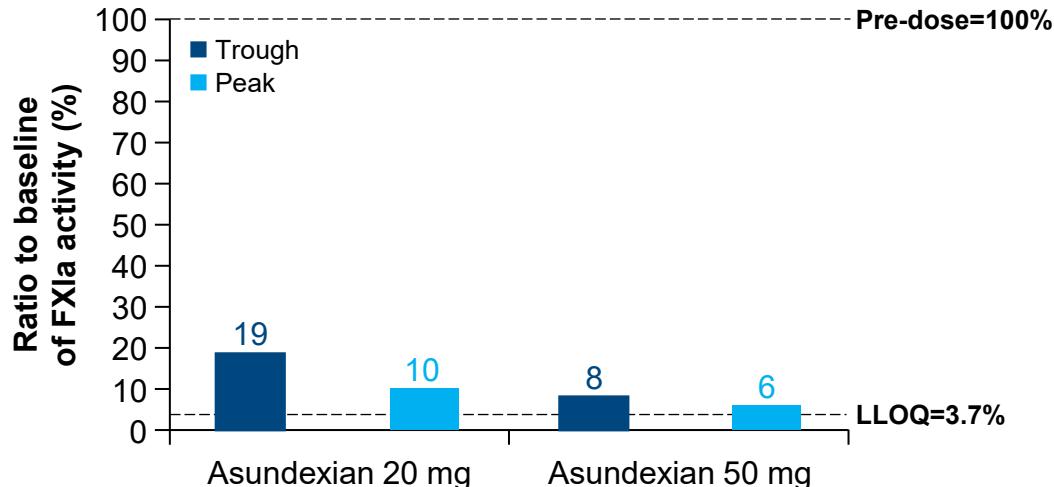
ASUNDEXIAN

- Direct oral inhibitor of FXIa^{1,2}
 - Once daily dosing
- No effect on bleeding time – alone or with DAPT
- Phase 2 studies >4000 participants showed^{3–6}
 - >90% inhibition of FXIa at peak and trough
 - No significant increase in major bleeding over placebo with or without antiplatelets

Safety of the oral factor XIa inhibitor asundexian compared with apixaban in patients with atrial fibrillation (PACIFIC-AF): a multicentre, randomised, double-blind, double-dummy, dose-finding phase 2 study



Jonathan P Piccini, Valeria Caso, Stuart J Connolly, Keith A A Fox, Jonas Oldgren, W Schuyler Jones, Diana A Gorog, Václav Durdík, Thomas Viethen, Christoph Neumann, Hardi Mundl, Manesh R Patel, on behalf of the PACIFIC-AF Investigators*



Reproduced from *The Lancet*, 399, Piccini JP, et al. Safety of the oral factor XIa inhibitor asundexian compared with apixaban in patients with atrial fibrillation (PACIFIC-AF): a multicentre, randomised, double-blind, double-dummy, dose-finding phase 2 study. 1383–90, Copyright (2026), with permission from Elsevier.

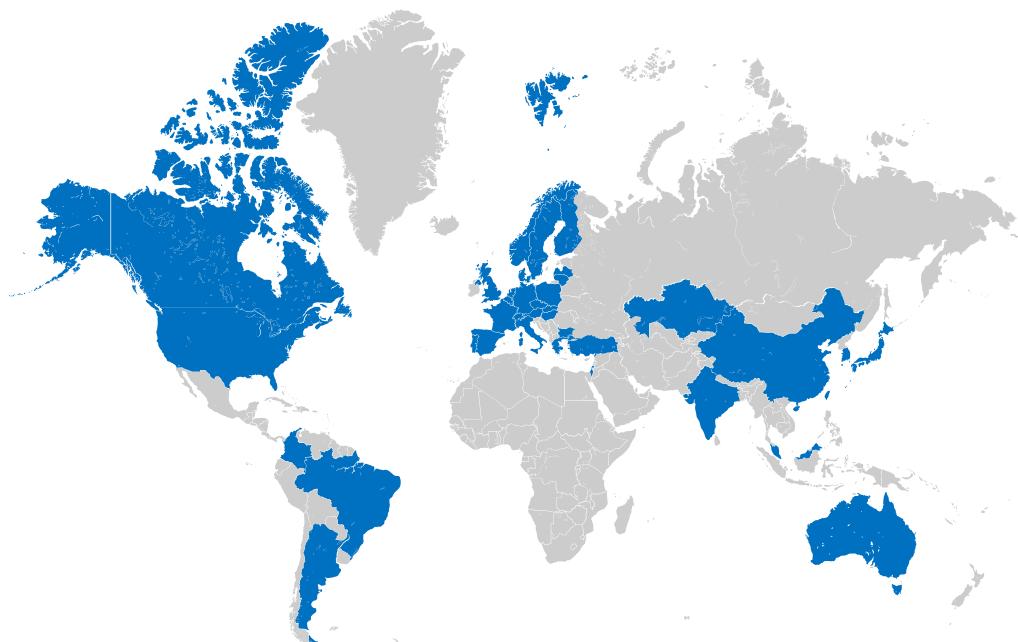
DAPT, dual antiplatelet therapy; FXIa, activated Factor XI.

1. Heitmeier S, et al. *J Thromb Haemost*. 2022;20(6):1400–11; 2. Piel I, et al. *Eur J Drug Metab Pharmacokinet*. 2023;48(4):411–25;
3. Rao SV, et al. *Circulation*. 2022;146(16):1196–206; 4. Piccini JP, et al. *Lancet*. 2022;399(10333):1383–90;
5. Shoamanesh A, et al. *Lancet*. 2022;400(10357):997–1007; 6. Eikelboom JW, et al. *J Am Coll Cardiol*. 2024;83(6):669–78.

OCEANIC-STROKE

Design

- OCEANIC-STROKE
 - Placebo-controlled
 - Double-blinded
 - Event-driven Phase 3 RCT
- Comparing asundexian 50 mg once daily and placebo
- Patients with non-cardioembolic stroke or high-risk TIA
 - Planned for antiplatelet therapy – single or aspirin + P2Y12 inhibitor (clopidogrel, ticagrelor, prasugrel)



37 Countries/Regions, 702 Sites

OCEANIC-STROKE: KEY ENDPOINTS

Endpoints (time to first occurrence)	
Primary efficacy*	Primary safety
Secondary efficacy*	Secondary safety
Ischemic stroke	ISTH major bleeding
<ul style="list-style-type: none">• All strokes (ischemic and hemorrhagic)• Composite of CV death, MI or stroke• Composite of all-cause mortality, MI or stroke• Ischemic stroke in the first 90 days• Disabling stroke (mRS ≥ 3 at 90 days)	<ul style="list-style-type: none">• Composite of ISTH major or CRNM bleeding• ISTH CRNM bleeding• Symptomatic intracranial hemorrhage• Hemorrhagic stroke• Fatal bleeding• Minor bleeding

*Hypothesis testing conducted using strict hierarchy order for efficacy endpoints.

CRNM, clinically relevant non-major; CV, cardiovascular; ISTH, International Society on Thrombosis and Haemostasis; MI, myocardial infarction; mRS, modified Rankin score.

KEY INCLUSION AND EXCLUSION CRITERIA

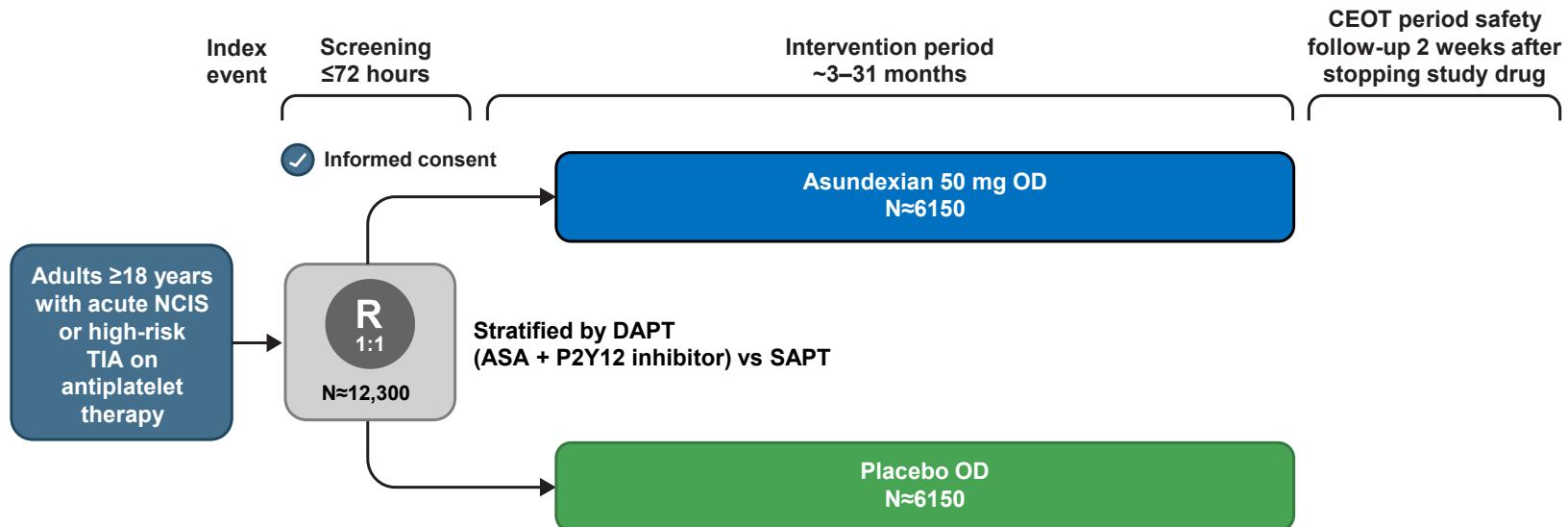
Key inclusion:

- Participants aged ≥ 18 years, within 72 hours of symptom onset:
 - Non-cardioembolic ischemic stroke (NIHSS ≤ 15) or high-risk TIA (ABCD² 6 or 7)
 - History of atherosclerosis or evidence of plaque on imaging or non-lacunar stroke on imaging
 - Plan for antiplatelet therapy, single or dual

Key exclusion:

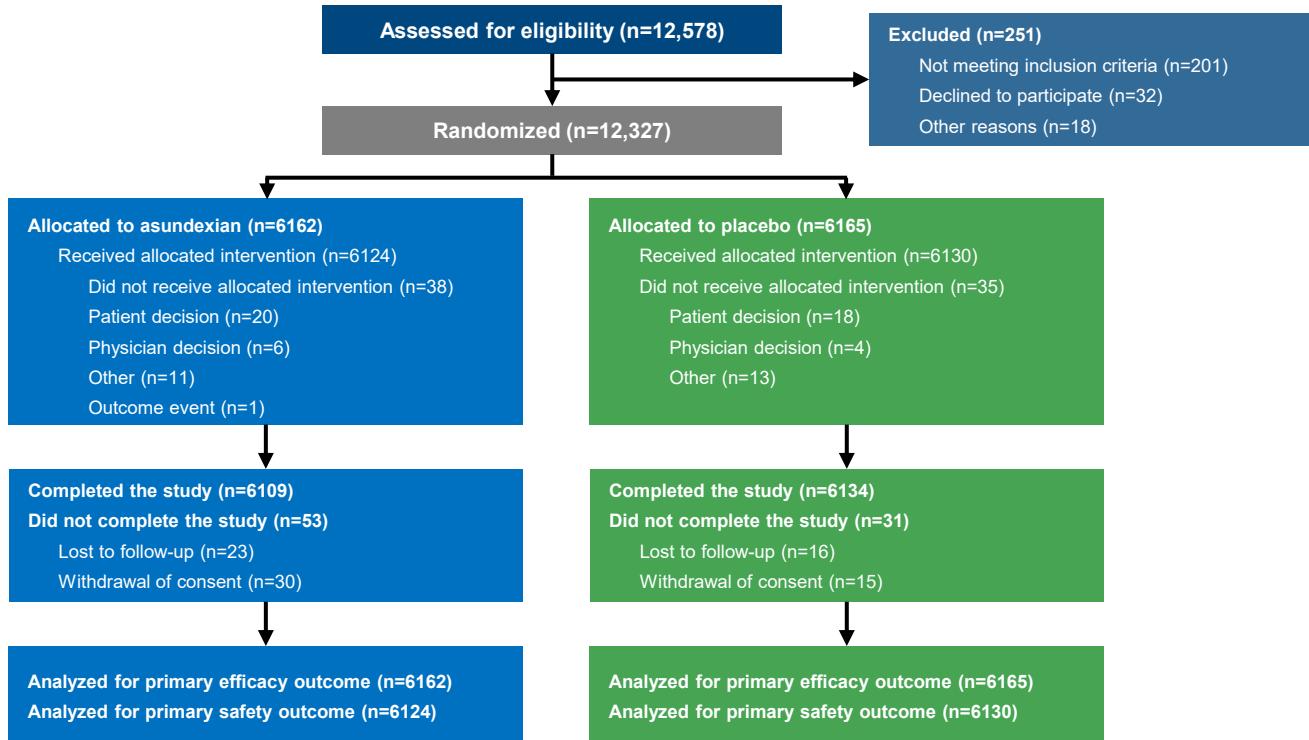
- History of AF or other cardioembolic source requiring anticoagulation
- Ischemic stroke within 7 days of index event
- Strokes following procedures (TAVI, CABG) or other specific cause (e.g. vasculitis)
- End-stage renal disease requiring dialysis
- Active non-trivial bleeding (e.g. PH1 or PH2); asymptomatic HT and CMB permitted
- History of non-traumatic ICH; significant GI bleeding within 6 months

OCEANIC-STROKE: STUDY DESIGN



ASA, aspirin; CEOT, common end of treatment; DAPT, dual antiplatelet therapy; NCIS, non-cardioembolic ischemic stroke; OD, once daily; P2Y12, purinergic receptor Y12; R, randomization; SAPT, single antiplatelet therapy; TIA, transient ischemic attack.
Sharma M, et al. Eur Stroke J. 2026;11(1):aakaf017.

CONSORT DIAGRAM



BASELINE CHARACTERISTICS

Characteristics	Asundexian 50 mg	Placebo
Randomized, N	6162	6165
Age, years, mean (SD)	67.7 (10.8)	67.5 (10.9)
Female sex, n (%)	2063 (33.5)	2047 (33.2)
Medical history, n (%)		
Previous history of stroke or TIA	1310 (21.3)	1345 (21.8)
Coronary artery disease	949 (15.4)	1013 (16.4)
Hypertension	4937 (80.1)	4868 (79.0)
Diabetes mellitus	2134 (34.6)	2115 (34.3)
Current smoker	1644 (26.7)	1665 (27.0)
Race, n (%)		
White	4105 (66.6)	4078 (66.1)
Asian	1721 (27.9)	1742 (28.3)
Black	143 (2.3)	139 (2.3)
Other	193 (3.1)	206 (3.3)

SD, standard deviation; TIA, transient ischemic attack.

INDEX EVENT CHARACTERISTICS

Characteristics	Asundexian 50 mg	Placebo
Index event, n (%)		
Ischemic stroke	5839 (94.8)	5838 (94.7)
High-risk TIA	323 (5.2)	325 (5.3)
TOAST subtype of index event,[†] n (%)		
Large-artery atherosclerosis	2512 (43.0)	2484 (42.5)
Stroke of undetermined etiology	1786 (30.6)	1710 (29.3)
Small-vessel occlusion	1290 (22.1)	1349 (23.1)
Stroke of other etiology	161 (2.8)	188 (3.2)
Cardioembolic	89 (1.5)	107 (1.8)
NIHSS at randomization,[†] median (IQR)	2 (1, 4)	2 (1, 4)
NIHSS at randomization,[†] n (%)		
≤3	4087 (70.0)	4079 (69.9)
4–7	1385 (23.7)	1375 (23.6)
≥8	365 (6.3)	382 (6.5)
Dual antiplatelet therapy	3859 (62.6)	3853 (62.5)

[†]Stroke index event only.

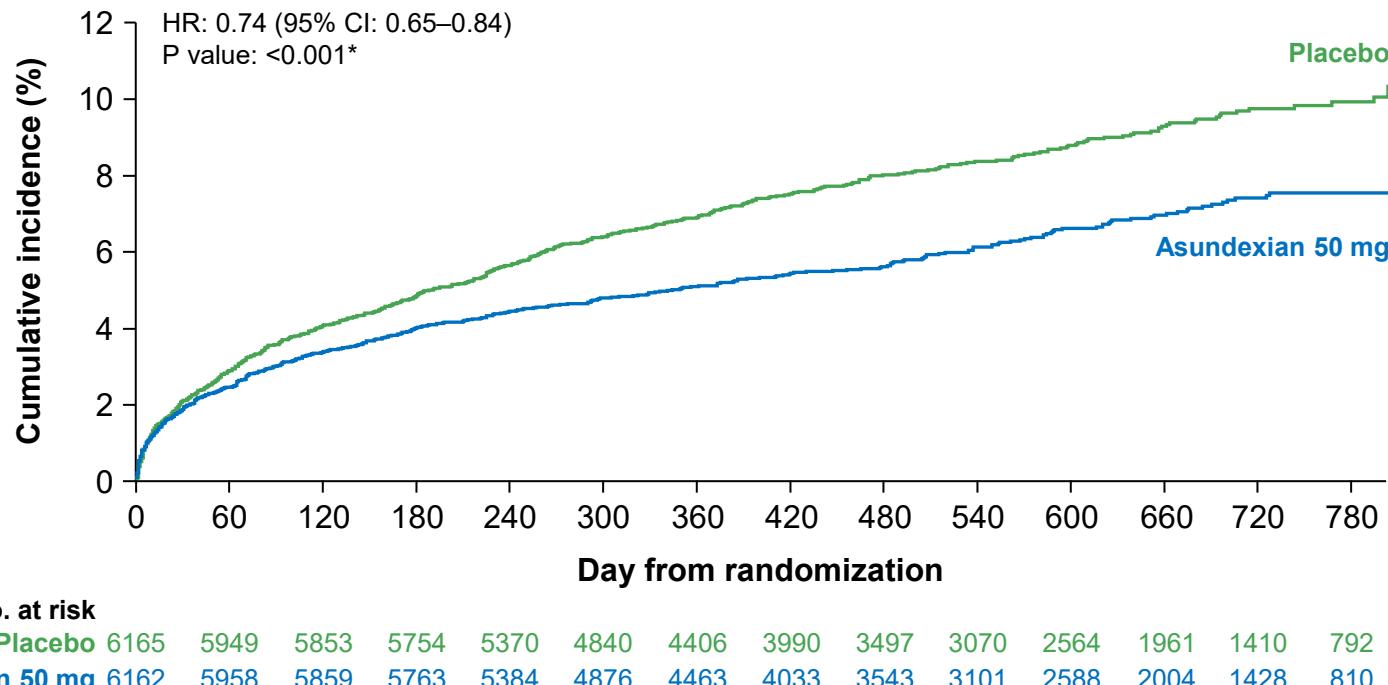
IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

ACUTE TREATMENT OF INDEX STROKE

	Overall N=11677	Asundexian 50 mg N=5839	Placebo N=5838
Intravenous thrombolysis and/or endovascular therapy,[†] n (%)	3201 (27.4)	1608 (27.5)	1593 (27.3)
Intravenous thrombolysis only	2314 (19.8)	1146 (19.6)	1168 (20.0)
Endovascular therapy only	371 (3.2)	202 (3.5)	169 (2.9)
Intravenous thrombolysis and endovascular therapy	516 (4.4)	260 (4.5)	256 (4.4)

[†]Stroke index event only.

CUMULATIVE INCIDENCE OF ISCHEMIC STROKE



*P value is obtained from stratified log-rank test (stratified by baseline intention of DAPT). csHR and 95% CI are provided here.

Absolute risk reduction at 1 year was 1.9%, with a number needed to treat of 53.

Cumulative incidence curves are estimated by Aalen-Johansen method, truncated at Day 820.

CI, confidence interval; csHR, cause-specific hazard ratio; DAPT, dual antiplatelet therapy; HR, hazard ratio.

EFFICACY OUTCOMES

Outcome	Asundexian 50 mg (N=6162)	Placebo (N=6165)	csHR (95% CI)†	P value‡
Primary efficacy event				
Ischemic stroke	384 (6.2)	518 (8.4)	0.74 (0.65–0.84)	<0.001
Secondary efficacy events				
All strokes (ischemic, hemorrhagic)	404 (6.6)	545 (8.8)	0.74 (0.65–0.84)	<0.001
CV death, MI or stroke	568 (9.2)	685 (11.1)	0.83 (0.74–0.92)	<0.001
All-cause mortality, MI, or stroke	649 (10.5)	757 (12.3)	0.85 (0.77–0.95)	0.003
Ischemic stroke in the first 90 days	183 (3.0)	218 (3.5)	0.84 (0.69–1.02)	0.08
Disabling/fatal stroke¶	128 (2.1)	185 (3.0)	0.69 (0.55–0.87)	Not applicable

†csHRs are estimated from stratified cox proportional hazard model (stratified by baseline intention of T); ‡P values are obtained from stratified log-rank test (stratified by baseline intention of T); ¶A disabling stroke is defined as a stroke of any type during the trial associated with a modified Rankin Scale (mRS) of ≥3 at 90 days after the stroke or an increase of 1 point if the last available mRS before the recurrent stroke event was ≥3.

csHR, cause-specific hazard ratio; CI, confidence interval; CV, cardiovascular; MI, myocardial infarction; mRS, modified Rankin score.

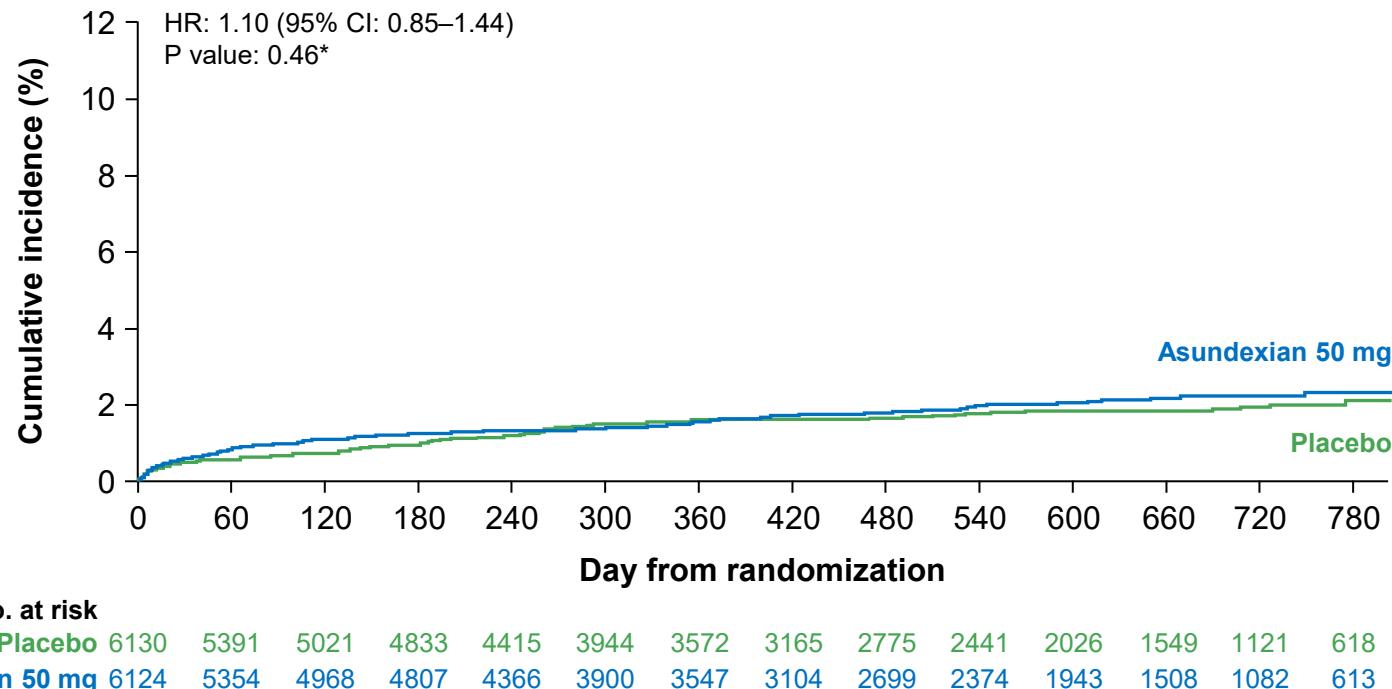
SAFETY OUTCOMES

Outcome	Asundexian 50 mg (N=6162)	Placebo (N=6165)	csHR (95% CI)†
n (%)	n (%)		
Primary safety event			
ISTH major bleeding	117 (1.9)	107 (1.7)	1.10 (0.85–1.44)
Secondary safety events			
ISTH major or clinically relevant non-major bleed	339 (5.5)	307 (5.0)	1.12 (0.96–1.30)
Clinically relevant non-major bleeding	231 (3.8)	210 (3.4)	1.11 (0.92–1.34)
Symptomatic intracranial hemorrhage (includes intracerebral hemorrhage)	41 (0.7)	36 (0.6)	1.15 (0.74–1.80)
Hemorrhagic stroke	13 (0.2)	20 (0.3)	0.66 (0.33–1.32)
Fatal bleeding	14 (0.2)	8 (0.1)	1.77 (0.74–4.23)
Minor bleeding	479 (7.8)	512 (8.4)	0.94 (0.83–1.07)

†csHRs are estimated from stratified Cox proportional hazards model (stratified by baseline intention of DAPT).

CI, confidence interval; csHR, cause-specific hazard ratio; DAPT, dual antiplatelet therapy; ISTH, International Society on Thrombosis and Haemostasis.

CUMULATIVE INCIDENCE OF ISTH MAJOR BLEEDING

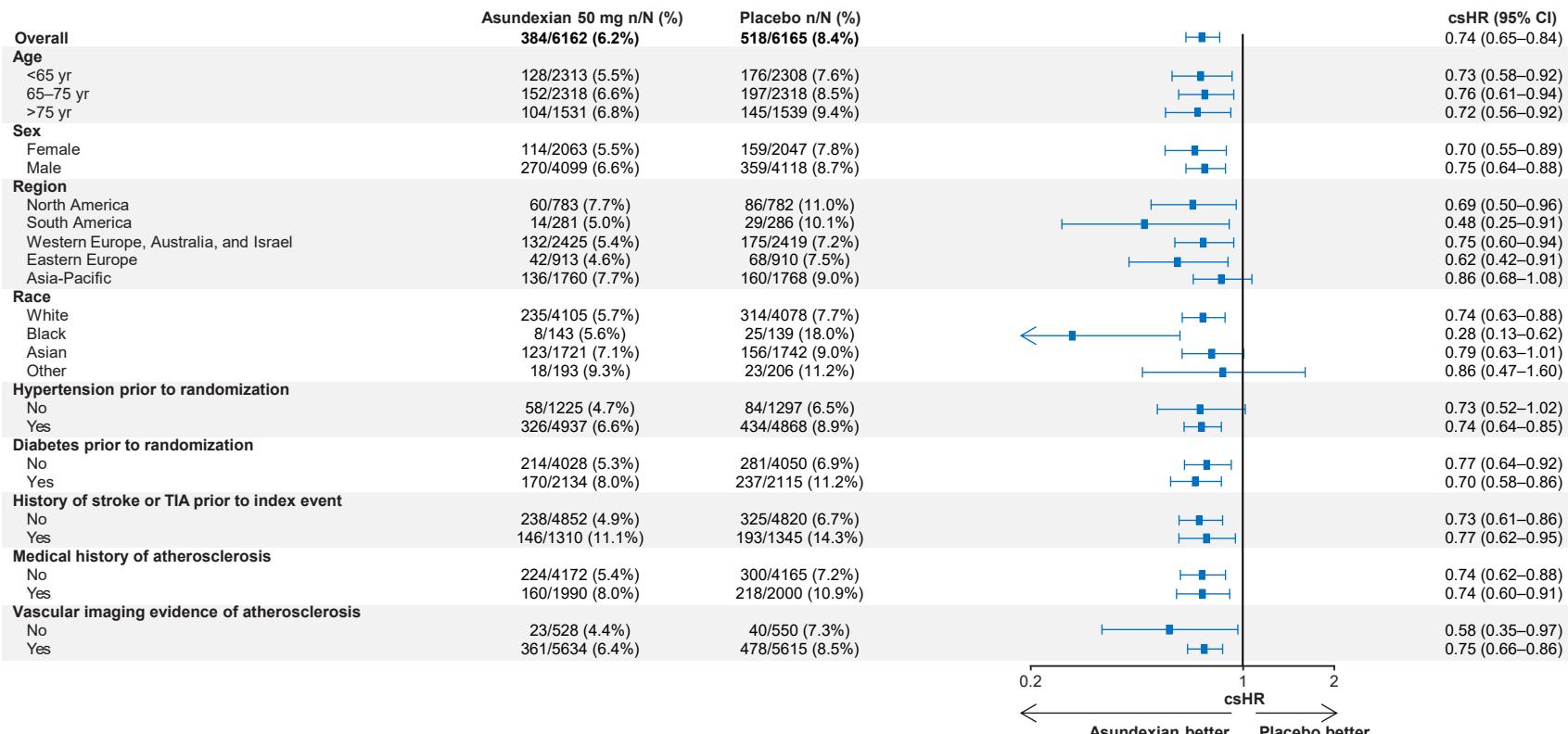


*P value is obtained from stratified log-rank test (stratified by baseline intention of DAPT). csHR and 95% CI are provided here.

Cumulative incidence curves are estimated by Aalen-Johansen method, truncated at Day 820.

CI, confidence interval; csHR, cause-specific hazard ratio; DAPT, dual antiplatelet therapy; HR, hazard ratio.

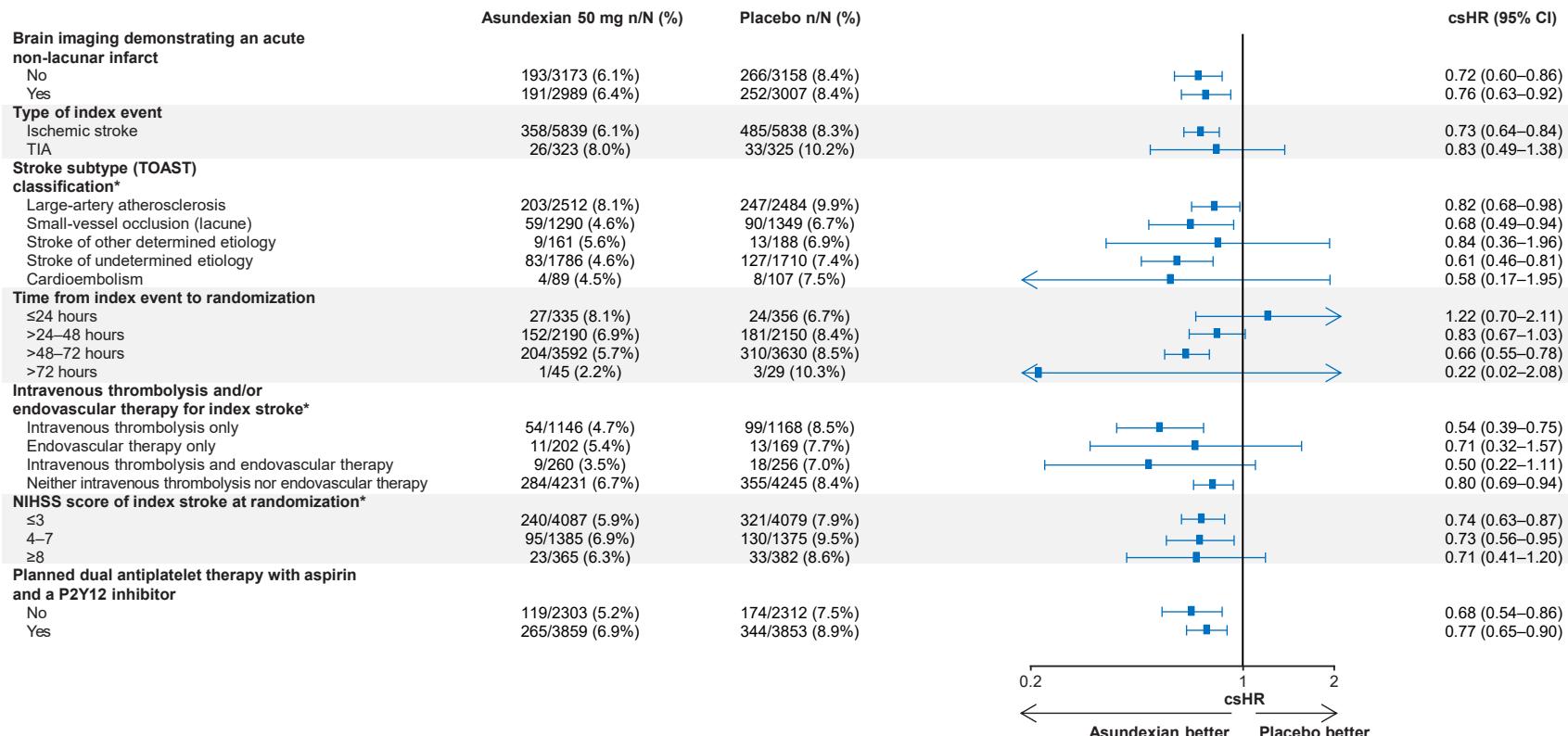
SUBGROUP ANALYSES FOR ISCHEMIC STROKE



CIs are unadjusted for multiplicity and may not be used for inference.

CI, confidence interval; csHR, cause-specific hazard ratio; TIA, transient ischemic attack.

SUBGROUP ANALYSES FOR ISCHEMIC STROKE



*For index event of ischemic stroke.

CIs are unadjusted for multiplicity and may not be used for inference.

CI, confidence interval; csHR, cause-specific hazard ratio; NIHSS, National Institutes of Health Stroke Scale; P2Y12, purinergic receptor Y12;

TIA, transient ischemic attack; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

CONCLUSION

- In patients with non-cardioembolic ischemic stroke or high-risk TIA treated with antiplatelet therapy, asundexian 50 mg reduced the occurrence of ischemic stroke (csHR 0.74; 95% CI, 0.65 to 0.84; $p<0.001$)
 - The difference between the treatment arms began early and continued throughout the treatment period.
 - A consistent effect was seen in subgroups.
- Asundexian was associated with a reduction in disabling or fatal stroke (mRS ≥ 3)
- Asundexian was not associated with an increase in bleeding
 - Including ISTH major,
 - CRNM, minor or intracranial bleeding

ACKNOWLEDGEMENTS

- This study was sponsored by Bayer AG
- Editorial support was provided by Prime Group of Companies (Knutsford, UK), funded by Bayer AG
- We thank the Steering Committee and independent Data Monitoring Committee members, the study operations teams, the investigators, the study site coordinators, and especially the patients and their families, who made this study possible

Steering Committee

Mike Sharma (Chair), Ashkan Shoamanesh (Co-Chair), Pierre Amarenco, Pablo Amaya, Sebastian Francisco Ameriso, Hee-Joon Bae, Daniel Bereczki, Bruce Campbell, Hanne Christensen, Charlotte Cordonnier, Jonathan Coutinho, Gian Marco De Marchis, Andrew Demchuk, Qiang Dong, John Eikelboom, Jose Ferro, Teruyuki Hirano, Fan Kee Hoo, Scott Kasner, Michael Knoflach, Martin Kovar, I-Hui Lee, Ronen Leker, Robin Lemmens, Arne Lindgren, Jaime Masjuan, Vaidas Matijosaitis, Evija Miglane, Robert Mikulik, Eva Muehlhofer, Hardi Mundl, Seref nur Ozturk, Jukka Putala, Tom Robinson, Gisele Sampaio Silva, Else Sandset, Jeff Saver, Kevin Sheth, Agnieszka Slowik, Ivan Staikov, PN Sylaja, Cristina Tiu, Georgios Tsivgoulis, Peter Turcani, Saule Turuspeкова, H. Bart van der Worp, Roland Veltkamp, Andrea Zini

Independent Data Monitoring Committee

Jonathan Halperin, Steven Greenberg, Thomas Cook, Saskia Middeldorp, Marta Rubiera del Fuego

THANK YOU

 **International**
Stroke
Conference

#ISC26



Scan QR code to view
this presentation

BASELINE CHARACTERISTICS

	Overall N=12327	Asundexian 50 mg N=6162	Placebo N=6165
Race, no. (%)			
White	8183 (66.3)	4105 (66.6)	4078 (66.1)
Black	282 (2.2)	143 (2.3)	139 (2.3)
Asian	3463 (28.1)	1721 (27.9)	1742 (28.3)
Other	399 (3.2)	193 (3.1)	206 (3.3)
USA race, no. (%)	1027	514	513
White	766 (74.6)	389 (75.7)	377 (73.5)
Black	194 (18.9)	94 (18.3)	100 (19.5)
Asian	24 (2.3)	7 (1.4)	17 (3.3)
Other	43 (4.2)	24 (4.7)	19 (3.7)